# Non-Technical Abstract

Ischemic heart disease (IHD) due to atherosclerosis is the most common underlying cause of cardiovascular disability and death in the US and Western World. The American Heart Association (AHA) estimates that 12.6 million Americans have IHD, and over 500,000 die from the disease every year. The lifetime risk of developing IHD after age 40 is 49 percent for men and 32 percent for women. The primary symptom of IHD is angina pectoris (pains in the heart). A number of approved medications including nitroglycerin, beta-adrenergic blocking agents, and calcium-channel blocking agents can improve symptoms by reducing myocardial oxygen demand, but no currently available medication can restore the compromised arterial blood supply. Invasive therapies and surgical procedures are reserved for high-risk patients and patients unresponsive to standard medical therapies.

Medical therapies for IHD are generally successful in controlling the symptoms of the disease, but even optimal therapeutic regimens do not prevent the eventual worsening of disease. One new approach to the treatment of IHD is therapeutic angiogenesis which induces of growth of new blood vessels in the heart. This approach to growing new blood vessels is the basis for this clinical trial.

The nature of HGF is similar to that of VEGF in that it stimulates the growth of new blood vessels which can restore blood flow to damaged areas of the heart. It is hypothesized that the localized expression of HGF produced from the AnGes gene transfer agent could contribute directly to the formation of new blood vessels in the heart. Therapeutic angiogenesis is considered a direct way to treat IHD by improving blood flow to the ischemic areas in the heart.

AnGes-MG, Inc. is currently evaluating HGF in patients with severe peripheral arterial disease (PAD) enrolled into the phase I/II study in Japan with 22 patients who have been treated safely with the product.

The initial phase I/II study for IHD in the US will have 2 stages. The first stage will be a dose-escalating safety study evaluating sequentially 4 doses of HGF DNA Plasmid (0.4 mg, 0.8 mg, 1.5 mg, and 4.0 mg) administered by intra-myocardial injections. In stage I of this trial, 8 patients will be evaluated at each of four dose levels; 6 patients will receive plasmid HGF and 2 patients will receive placebo. Three doses with acceptable safety will be compared to placebo in stage II section of the clinical study. In stage II of the clinical study up to 60 patients will be randomized to either placebo or one of 3 doses of plasmid HGF. It is anticipated that the stage II design of this study will assess the safety of the three doses and provide some initial data regarding the effect of plasmid HGF on improved perfusion in the ischemic area of the heart. Results from this phase I/IIa trial will help determine the design of additional trials to further evaluate the safety and clinical effect of this gene transfer agent in IHD patients.